UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/672,020	09/29/2000	Thomas J. Gardella	0609.4820002/SRL/TBB	2982

26111 7590 06/19/2003

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/672,020	GARDELLA ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *3-7 and 13-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Claims 3-7, 13-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 9, 4/2/2003. Claims 1-2, 8-12 are under consideration.

Claim Objections

Claims 8-9 are objected to because of the following informalities: They contain limitations drawn to non-elected Groups. Appropriate correction is required.

In addition, claim 8 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must be written strictly in the alternative. See MPEP § 608.01(n). Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 8-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide with the amino acid sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for a variants of SEQ ID NO: 1 as set forth in claim 1, or polypeptides having an amino acid sequence at least 90% identical to SEQ ID NO: 1 or the variants set forth in claim 1, or fragments of SEQ ID NO: 1, or fragments of the

variants of SEQ ID NO: 1 as set forth in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.

In the instant case, the claims encompass variants of SEQ ID NO: 1 as set forth in claim 1, polypeptides having an amino acid sequence at least 90% identical to SEQ ID NO: 1 or the variants set forth in claim 1, and fragments of SEQ ID NO: 1 or fragments of the variants of SEQ ID NO: 1 as set forth in claim 1. Thus, the claims encompass many variant proteins. Applicant has only taught the amino acid sequence of SEQ ID NO: 1. Additionally, the claims do not recite a functional limitation. While the specification provides adequate guidance for making SEQ ID NO: 1, and provides adequate teaching on how to make other polypeptides with a similar sequence, the specification fails to provide guidance on use of the variant polypeptides. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding

site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. For example, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Thus, the amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the encoded proteins are lacking, it is unpredictable as to which polypeptide variations, if any, meet the limitations of the claims.

Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of SEQ ID NO: 1. Therefore, while the specification provides the necessary guidance to make the polypeptides set forth in SEQ ID NO: 1 and variants, it does not provide the necessary guidance for one of skill in the art to use the polypeptides. Further, since no functional language is associated with the polypeptides of SEQ

ID NO: 1 or variants, one of ordinary skill in the art would not know how to use these defined sequences except in further characterization of the sequences themselves. Due to the large quantity of experimentation necessary to generate the large number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim 12 encompasses a pharmaceutical composition of the polypeptide of claim 1, which encompasses variants of SEQ ID NO: 1 as set forth in the claim. As set forth above, Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of SEQ ID NO: 1. Therefore, while the specification provides the necessary guidance to make the polypeptides set forth in SEQ ID NO: 1 and variants, it does not provide the necessary guidance for one of skill in the art to use the polypeptides, and hence does not provide sufficient guidance for a pharmaceutical composition of the variant polypeptides. Further, since no functional language is associated with the polypeptides of SEQ ID NO: 1 or variants, one of ordinary skill in the art would not know how to use these defined sequences except in further characterization of the sequences themselves. Since in order for a composition to be considered pharmaceutical, there must be a condition that the composition would treat. In the instant case, the Specification only sets forth that the

polypeptide of SEQ ID NO: 1 was active in cells expressing the PTH-2 receptor and in osteoblast cells, however, there is not a correlation between these activities and the treatment of a disease state, and since there is no activity associated with the variant polypeptides, it would require one of skill in the art to determine the function of the variant polypeptides, then determine whether this function would correlate to the treatment of a disease state, thus requiring undue experimentation.

Given the breadth of claims 1-2, 8-12 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Claims 2, 8-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims encompass polypeptides having an amino acid sequence at least 90% identical to SEQ ID NO: 1 or the variants set forth in claim1, and fragments of SEQ ID NO: 1 or fragments of the variants of SEQ ID NO: 1 as set forth in claim 1. Thus, the claims encompass variant proteins, while Applicant has only taught SEQ ID NO: 1. The specification and claim do not indicate what distinguishing attributes shared by the members

of the genus. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

The closest prior art found is Luck et al. (1999). Luck et al. teach fragments of parathyroid hormone which bind the PTH-1 receptor and stimulate camp production. Luck et al. teach that the peptides contain a C-terminal amide (page 677, column 2, second full paragraph). Luck et al. further teach polypeptide fragments of PTH wherein the peptide consists of amino acids 1-9 and 1-10, 1-11, 1-12 and 1-13 of SEQ ID NO: 1 (page 671, Figure 1). Luck et al. further teach radiolabeled peptides comprising the fragments, (see page 676, Figure 7). While Luck et al. do not teach the exact sequence of claim 1, $AVAEIQLMHX_{01}X_{02}X_{03}KX_{04}$, they do teach the sequence AVAEIQLMHALAK(H or A). The difference is that claim 1 is drawn to a polypeptide wherein X_{04} is either phenylalanine or tryptophan, whereas the polypeptide of Luck et al. has either a histidine or alanine at the corresponding position.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
June 18, 2003

Gary L Kunz
GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600